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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,431	07/27/2006	**Hikaru Kai**	09864/0207778-US0	4903

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DARBY & DARBY P.C.
P.O. BOX 770
Church Street Station
New York, NY 10008-0770

EXAMINER	
BLUMEL, BENJAMIN P	
ART UNIT	**PAPER NUMBER**
1648	

MAIL DATE	DELIVERY MODE
10/14/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,431	KAI ET AL.	
	Examiner	Art Unit	
	BENJAMIN P. BLUMEL	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *7/27/06* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/13/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Applicants are informed that the rejections of the previous Office action not stated below have been withdrawn from consideration in view of the Applicant's arguments. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-3 and 7 are examined on the merits.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 7/23/2009 was filed after the mailing date of the final Office action on 4/28/2009. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Response to Arguments

Applicant's arguments filed 7/27/09 have been fully considered but they are not persuasive. See responses below.

Claim Rejections - 35 USC § 103

(New Rejection) Claims 1-3 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kistner et al. (Developments in Biological Standardization, 1999), Wang and Ouyang (Bioprocess Engineering, 1999), Aerts et al. (US PGPub 2006/0183224 A1) and Kobatake et al. (Biotechnology Techniques, 1999).

The claimed invention is drawn a method of producing a virus comprising: adhering adhesive cells to a microcarrier which has a polypeptide (P) having 4 to 50 cell-adhesive

minimum amino acid sequences (X) per molecule and 4 to 51 auxiliary amino acid sequences (Y), and is free from animal-origin components; culturing the adhesive cells in a medium free from animal-origin components; subculturing the cultured adhesive cells using a cell dispersing agent free from animal- origin components; and then inoculating and proliferating a virus in the cells obtained by culturing the adhesive cells. The virus produced belongs to at least one selected from a group consisting of *Flaviviridae, Orthomyxoviridae, Adenoviridae, Herpesviridae, Picornaviridae, Paramyxoviridae, Togaviridae, and Poxviridae.* In the present invention, "free from animal origin components" means free from components originated from homoeothermic animals, in particular, animals such as mammals (for example, human, cattle, pig, dog, rabbit, cat, and the like), birds, and fishes. *See page 4 lines 1-3 of specification).*

Kistner et al. teach producing influenza viruses in Vero cells attached to microcarriers (Cytodex-3) which contain denatured collagen (a natural cell binding protein) [as evidenced by Wang and Ouyang, page 207] with serum-free media. Kistner et al. use a porcine trypsin enzyme during the culture process of the virus. Even though collagen is a protein of animal origin, the denatured form of the collagen employed by Kistner et al. is structurally distinct from that of a naturally occurring collagen molecule and therefore not of animal origin. However, Kistner et al. do not teach the involvement of an auxiliary amino acid sequence as part of the polypeptide (P) which as defined in the specification, aids in the thermal stability of P; or the use of a cell dispersing agent that is free of animal origin components. *See pages 103, 106 and table 5.*

Aerts et al. teach the importance of culturing viruses (including influenza virus) in media that lacks components from animals (i.e., sera and proteases). As a result, Aerts et al. teach that

after the cells (such as Vero) have been cultured on a substrate, rProtease or Trypzean (proteases) can be used to release the attached cells during harvest. These recombinant proteases are produced by bacteria or plants, thereby being free of animal components (i.e., infectious agents, etc.). In addition, the media used for culturing cells should be serum-free (i.e., free from animal components). *See paragraphs 14, 20, 40 and 61.*

Kobatake et al. teach how to introduce specific amino acids residues into a cell attachment protein for adhering cells in tissue culture protocols. These residues (APGVGV) improve the stability of the attachment protein as demonstrated by retaining over 90% of its cell adhesion properties following autoclave treatment, while fibronectin lost approximately 50% of its binding capability under the same conditions. Therefore, Kobatake et al. provide an improve tissue culture method that would allow for maintaining cell adherent surfaces following extreme temperature conditions. *See page 24 and figure 3.*

It would have been obvious to one of ordinary skill in the art to modify the methods taught by Kistner et al. in order to modify a cell attachment protein containing auxiliary amino acid sequences, which improve thermal stability and the use of non-animal source cell dispersion components can reduce the risk of animal contaminates being introduced into a viral preparation. One would have been motivated to do so, given the suggestion by Kistner et al. that the method be used to efficiently propagate viruses in microcarrier tissue cultures. There would have been a reasonable expectation of success, given the knowledge that recombinant proteases from non-animal sources can be used in culturing cells in virus productions as taught by Aerts et al., and also given the knowledge that existing cell attachment proteins can be modified by inserting short amino acid sequences resulting in an increased thermal stability, as taught by Kobatake et

al. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments:

Applicant's argue that the examiner's interpretation of "free from animal-origin components" is incorrect because Kistner et al. employ denatured collagen originally from an animal. In addition, it is argued that the examiner has ignored the limitations of using culture media that is free form animal origin components and cell dispersing agent that is also free form animal-origin components since porcine (i.e., Pig) trypsin from Sigma was also used by Kistner to disperse the cells. It is also argued that since sample 4 (cytodex 1 bead with ProNectin protein) achieved a higher ELISA result and HA titer when compared to sample 3 (cytodex 3 bead with denatured pig collagen), the teachings of Kistner et al. would not result in an increase of virus production by using the presently claimed invention.

In response, while Kistner et al. use a porcine derived trypsin (isolated from animal), Aerts et al. teach the importance of using non-animal proteases for cell dispersion (such as rProtease) when culturing viruses. In addition, while the collagen used by Kistner et al. originally came from a pig, the examiner maintains that its denaturing results in a product which meets the key feature of the claimed invention being present (i.e., free from animal components such as infectious agents, or other contaminating foreign substances) based on the further characterization on pages 4 and 5 (abridging paragraph).

In addition, applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., improved viral production) are not recited in the rejected claim(s). Although the claims are interpreted in light

of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BENJAMIN P. BLUMEL whose telephone number is (571)272-4960. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/BENJAMIN P BLUMEL/
Examiner
Art Unit 1648

/Gary B. Nickol /
Supervisory Patent Examiner, Art Unit 1646